REMARKS

Applicants note that upon filing the RCE the Examiner has entered the amendments submitted on October 21, 2005 as well as the amendments submitted on November 22, 2005 accompanying the request for an RCE. The amendments submitted on November 22, 2005 were intended to be a substitute for the amendments previously submitted on October 21, 2005. The amended claims sets for the October 21, 2005 and November 22, 2005 submissions were identical with the exception of the amendment to claim 21. To avoid any confusion regarding the status of that claim, applicants have canceled claims 21 and 22 and have resubmitted those claims as new claims 23 and 24 herein. New claim 23 further states that the capillary tube wall is about 0.1 mm thick or less.

Claim 21 stands rejected under 35 USC § 103 as being unpatentable over von Behrens (US 3,914,985). Applicants respectfully traverse this rejection.

Claim 21 employs the transitional language "consisting of" and thus the claimed device excludes the additional structures that comprise the von Behren's device. The Examiner agrees that the von Behrens device includes additional structure, but contends that such structure is only required when supporting the inner tube within a centrifuge device. The Examiner contends that it would be obvious to provide the inner tube as a separate structure from the other elements described in the invention of von Behrens because one could use this component (i.e. the inner tube) as a starting material to construct the actual device disclosed in von Behrens.

Applicants respectfully submit that the simple fact that a portion of a known device could be manufactured as a component for constructing the larger more complex device cannot provide the sole basis of obviousness of the component part as a separate entity. The Examiner speculates that the inner tube could be provided as a separate structure to allow the use of "off

the shelf-type of outer tubes" with the disclosed inner tube. Such speculation, finding no support within the von Behrens reference, ignores the fact that the inner tube is "relatively fragile" (see column 3, line 5 of von Behrens) and thus manufacturing and storing the inner tube as a separate component would run the unnecessary risk of breakage. Applicants respectfully submit the Examiner must provide some teaching or suggestion regarding the desirability of preparing such an "inner tube device" in the absence of the disclosed additional structure, other than mere speculation that such a device could serve as a component to make the actual disclosed device.

This is particularly true in the present case wherein the von Behrens reference clearly teaches a functional interrelationship between the additional structures and the single component on which the Examiner wishes to focus. Von Behrens clearly teaches the desirability of an interflow between the cell-free liquid within the outer tube and the blood or other fluid contained within the inner tube (see column 2, lines 43-51). Thus the outer tube does more than simply provide support to the inner tube, it also holds a liquid that maintains the hydrostatic equilibrium of the system (see Fig. 11, column 3, lines 5-15, column 7, lines 1-16). There are simply no drawings demonstrating an empty inner tube as a stand alone component without the additional structures, or a teaching or suggestion of a device that consists solely of the inner tube, or that such an embodiment would serve any purpose. The Examiner notes that von Behrens mentions the possibility of sealing one end of the capillary section of their device, but again this embodiment is provided for the specific expressed purpose of preventing an exchange of between the contents of the inner and out tubes (not for the elimination of the additional structure), and in fact the corresponding drawing (Fig. 6) shows the presence of the outer tube with this embodiment. Therefore, at no time did the von Behrens reference suggest a device that

consists solely of the inner tube portion of their device, or that such a component would have any value outside its combination with the outer tube.

The teaching of von Behrens simply fails to provide any motivation to prepare a stand alone device that consists of a receiving portion defining a first internal volume and a reaction portion, consisting of a capillary tube that is closed at one end and has a capillary tube wall about 0.1 mm thick or less, wherein the capillary tube volume is less than the first volume of the receiving portion and not greater than 100 μℓ.

Furthermore, claim 21 has been amended to specify that the thickness of the capillary tube wall is 0.1mm or less. The von Behrens reference is silent regarding the thickness of the walls of the disclosed containers and is devoid of any suggestion regarding the use of a vessel comprising a capillary tube having walls as thin as 0.1mm. Accordingly, even assuming that a device consisting only of the inner tube of von Behrens would be an obvious derivative of the von Behrens's device (which applicants respectfully submit it is not), the von Behrens teaching still fails to teach or suggest the invention as a whole as claimed herein including the specified thin walled capillary portion.

Claims 1-3, 5, 6, 9-11, 15, 21 and 22 stand rejected under 35 USC 103 as being unpatentable over von Behrens (US 3,914,985) in view of Fite et al (US 5,142,143). Applicants respectfully traverse.

The inadequacies of the von Behrens reference in regards to the presently claimed invention have been described above, including von Behrens failure to teach or suggest a container having the designated thin capillary walls. The Examiner has cited the Fite et al reference for establishing that capillary tubes were known that have a wall thickness similar to the wall thickness of the capillary portion of applicants' claimed device. However, applicants

respectfully submit that the prior art is full of many examples of capillary tubes having varying dimensions including varying degrees of capillary wall thickness. As evidence of the various capillary vessels that are commercially available, applicants have attached hereto Exhibits A -C, disclosing capillary tubes having wall thickness of 0.2mm (Exhibit A), 0.2mm (Exhibit B), and 0.175 and 0.5mm (Exhibit C). Similarly, US patent no. 5,315,673 discloses a self declared "thin walled" glass capillary tube having the dimensions: 75 mm long, 1.2 mm O.D., 0.2 mm wall thickness (see Example 1, line 7). All of these capillaries are well outside the size range of the present invention. This is not intended to be an exhaustive list but rather a sampling of the wide variety of capillaries from which a skilled practitioner has to choose from when selecting a capillary tube for use in an invention. The Examiner has cited one reference (Fite et al) that happens to disclose a capillary tube having a thin walls similar to applicants' disclosed capillary wall thickness. However the Examiner has failed to providing any motivation for selecting this particular capillary for combination with the von Behrens device in light of the many other capillary vessels from which to choose.

Von Behrens is entirely silent regarding the thickness of their capillary walls and provides no motivation for selecting the capillary disclosed in Fite et al over other capillaries having different dimensions. This is because the thickness of the capillary wall has absolutely no bearing on the functionality of the von Behrens device. Thus there is simply no motivation for modifying the device of von Behrens to include the specific capillary tube disclosed in Fite. On the contrary, due to the susceptibility of thin walled capillaries to breakage there was a reason why the capillary portion of von Behrens would be selected to have walls thicker than 0.1 mm. The issue of breakage is a real concern as indicated in attached Exhibit D and the marketing of unbreakable plastic capillary tubes. Accordingly, absent some teaching to the contrary a skilled

practitioner would be motivated to use capillaries having thicker walls rather than thinner ones as suggested by the Examiner to moderate problems associated with breakage.

Unlike the device disclosed in von Behrens, the claimed containers of the present invention have been designed to optimize the transfer of thermal energy to and from a sample contained within the container. Thus the thickness of the vessel walls, as well as the material comprising the vessel, have a direct bearing on the functionality of the presently claimed containers, which are designed for use in rapid thermal cycling reactions. The thickness of the capillary walls of applicants' device is one important element of the claimed vessels that have been designed for optimal thermal transfer while allowing fluoresecent monitoring of a PCR reaction contained in the container. Accordingly, the elevated risk of container breakage is accepted in exchange for the container having the optimal thermal energy transfer properties.

The sample container of the present invention has been designed to provide for the rapid and homogenous thermal cycling of the container contents. The ability to rapidly thermal cycle a sample allows one to conduct nucleic acid amplifications in a shorter length of time, and has been found to increase the yield and specificity of the polymerase chain reaction relative to prior art methods. Furthermore, the containers of the present invention have been designed to allow real time monitoring of the amplification reaction by monitoring fluorescent emitted from the end tip of the container. As demonstrated in Fig. 22A, detecting fluoresence emitted from the end tip of the container provides a 10 fold increase in signal intensity relative to detecting fluoresecence emitted from the side of the container.

Accordingly, the claimed containers of the present invention represent a unique combination of elements that allows for optimal rapid thermal cycling of a sample placed within the container. The motivation for combining these separate and distinct elements to form

applicants' novel container derives from applicants' discovery of the beneficial results in yield and specificity (see data of Figs. 6, 7 and 9) produced by conducting rapid cycling PCR. Absent applicants' discovery of the advantages of conducting rapid thermal cycling there was simply no motivation to prepare the empty containers of the present invention having a capillary portion with capillary walls only 0.1 mm thick. The Examiner has failed to provide sufficient motivation for why one would modify the von Behrens device by incorporating the specific capillary tube disclosed in Fite, rather than using any of the other capillary tubes available in the art. The Examiner cannot selectively pick and choose elements from the prior art to arrive at the claimed invention absent a convincing line of reasoning as to why such a selection would have been obvious. Ex parte Clapp, 227 USPQ 972 (BPAI 1985). Accordingly, applicants respectfully submit the Examiner has failed to establish a prima facie case of obviousness.

Accordingly, applicants respectfully request the withdrawal of the rejection of claims 1-3, 5, 6, 9-11, 15, 21 and 22 for obviousness under 35 USC 103.

Claim 4 stands rejected under 35 USC 103 as being unpatentable over von Behrens (US 3,914,985) in view of Fite et al (US 5,142,143) taken further in view of Gerarde (US 3,518,804). Applicants respectfully traverse.

Claim 4 depends form claim 1 and therefore the subject matter of this claim is patentable over the disclosures of von Behrens and Fite for the reasons stated above. The Gerarde reference fails to supplement the inadequacies of the von Behrens and Fite references as described above. Gerarde is directed to a capillary fill device. The present invention includes an empty capillary tube that is closed at one end, and a stopper removably inserted into the receiving portion of the container. The container of claim 4 is believed to be patentable over the

cited combination of references and applicants respectfully request the withdrawal of the rejection of claim 4 for obviousness.

Claims 12 and 20 stands rejected under 35 USC 103 as being unpatentable over von Behrens (US 3,914,985) in view of Fite et al (US 5,142,143) taken further in view of Hawes (US 3,556,659). Applicants respectfully traverse.

The inadequacies of the von Behrens and Fite teachings have been discussed previously. In addition, applicants respectfully submit there is no motivation provided within the von Behrens or the Gerarde references that would direct one of ordinary skill to consider the optical characteristics of their devices. The references are devoid of any suggestion that their device could be used with optical interrogation devices. Accordingly, there is no motivation to combine the teaching of Hawes (relating to laser-excited raman spectrometers) with the teaching of von Behrens and Fite.

The Examiner has cited the disclosure of Hawes for the premise that it is conventional in the art to seal the end of a capillary tube such that it forms a flat tip. Applicants note that nowhere within the text of Hawes do the inventors discuss a "capillary tube with a flat tip." Furthermore, applicants note the drawings referenced by the Examiner show that the end of capillary tube is provided with a convexed lens. Thus the objective teaching of Hawes states that for optical measurements of the content of a capillary vessel, the end of the vessel should be convexed. Accordingly, the Hawes reference does not provide motivation to form a container consisting of a receiving portion and a reaction portion, wherein the reaction portion consists of a capillary tube that is closed at one end with a flat tip.

Presumably the flattened end referred to by the Examiner was provided simply to allow the attachment of the convexed lens to the end of the capillary tube portion. There is

simply no suggestion that would motivate one to prepare a flat ended capillary tube by itself in the absence of additional structure. The very fact that Hawes teaches the need for attaching a convexed lens to their capillary tubes would actually suggest the opposite, that the end of the capillary tube should comprise a curved structure. Therefore, the invention of claims 12 and 20 is believed to be patentable over the cited references and applicants respectfully request the withdrawal of the rejection of those claims.

The foregoing claim amendments and remarks are believed to fully respond to the Examiner's rejections and the claims are believed to be in condition for allowance. Applicants respectfully request allowance of the claims, and passage of the application to issuance. If any further discussion of this matter would speed prosecution of this application, the Examiner is invited to call the undersigned at (434) 220-2866.

Respectfully submitted,

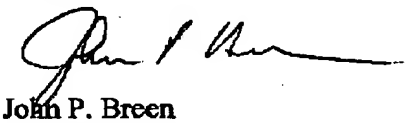

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Exhibit A

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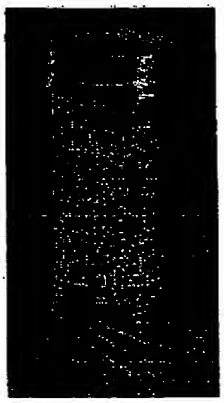
Fisherbrand* Microhematocrit Capillary Tubes

Low-taper wall construction guarantees error less than 1% absolute, 0.4 hematocrit, relative

- Ends can be sealed by flame, or sealing clay
- Manufactured from low-taper, soft glass
- Red band on tube indicates heparinization; blue band indicates nonheparinized tube
- Interior surface of heparinized tubes is evenly coated with ammonium heparin (4 to 7 USP units), which will not interfere with sodium determination
- Length: 75mm±0.02mm
- Inner diameter: 1.1 to 1.2mm
- Wall: 0.2mm ±0.02mm
- Capacity: 70µL
- Taper does not exceed 0.0254 mm in 75 mm
- Available plain or heparinized with not less than 2 USP units of ammonium heparinate
- Color-coded tube tips and labels
- Packaged in Fisher shaker-top vials for ease in dispensing
- 200 tubes per vial



22-362-566

More Details

Characteristics	Cat. No.	Qty.	Price
Tube, Capillary, Fisherbrand; Microhematocrit; Heparinized; 75mm±0.02mm L; 70µL; Red; low-taper, soft glass; ends sealed by flame; color-coded tube tips and labels; 200 tubes per vial	22-362-566		(•) Pack of 200 for $22.72 ( ) Case of 5 for $94.65 Add To Shopping Cart
Tube, Capillary, Fisherbrand; Microhematocrit; Plain; 75mm±0.02mm L; 70µL; Blue; low-taper, soft glass; ends sealed by flame; color-coded tube tips and labels; 200 tubes per vial	22-362-574		(•) Pack of 200 for $21.39 ( ) Case of 5 for $89.13 Add To Shopping Cart

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Exhibit B

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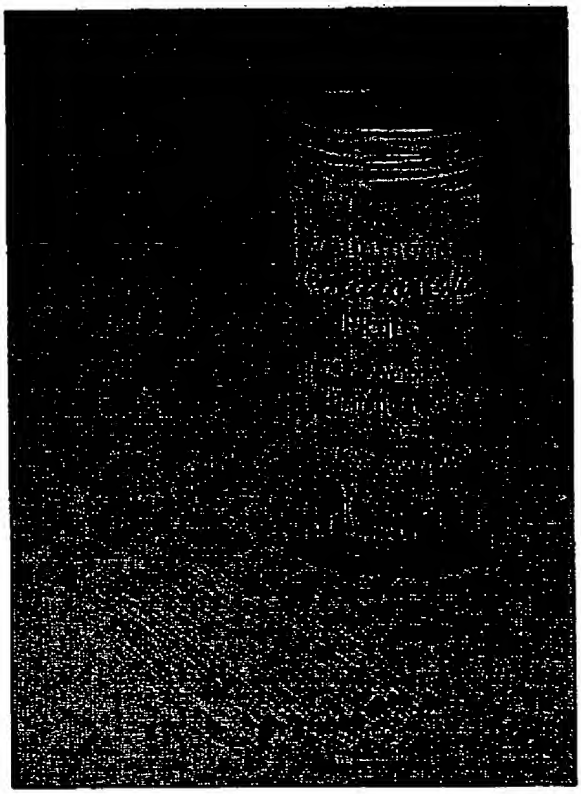
Hemato-Clad* Mylar*-Wrapped Hematocrit Tubes

Combine the precision of glass with the safety of Mylar wrapping

Fisher HealthCare Catalog > Specimen Collection > Blood Specimen Collection > Tubes for Blood Collection > Microhematocrit Tubes > Hemato-Clad* Mylar*-Wrapped Hematocrit Tubes > Details

- The chance of contamination due to glass fragments or aerosols is greatly reduced
- Accidental breakage is significantly reduced, particularly when pressing into clay sealant (not included)
- In the event of breakage, the Mylar* wrapping will help contain the blood sample and provide an added layer of protection against cuts from broken glass
- Available both plain and heparinized



21-176-5

Type	Color Code	Inside Diameter	Tube Length	Wall Thickness	Cat. No.	Qty.	Price
Heparinized	Red	1.1 to 1.2mm	75mm	0.2mm	21-176-6		Pack of 200 fo $13.75 Case of 5 for $60.85
Plain	Blue	1.1 to 1.2mm	75mm	0.2mm	21-176-5		Pack of 200 fo $12.46 Case of 5 for $55.15

Add Item(s) To Shopping Cart

Exhibit C

GLASS
MICRO HEMATOCRIT TUBES

Plain and Heparinized:

- 75 mm Length
- 75 µl Volume
- Inner Diameter: 1.15
- Outer Diameter: 1.5
- Fire-Polished Tips

Color Codes:

- Untreated - Blue Tip
- Ammonium Heparinized - Green Tip

Packaging:
100 tubes per vial - 10 vials per box
(1000 tubes per box)

Pre-Calibrated:

- 75mm Length
- 18µl Volume
- Inner Diameter: 0.55
- Outer Diameter: 1.55
- Calibration line at 60mm from one end
- Black calibration line establishes a uniform blood column length
- Treated with ammonium heparin

Packaging:
100 tubes per vial - 10 vials per box
(1000 tubes per box)

Capillary Tube Specimen Holding Tray with Sealant:

- Unique wax compound quickly forms a leak-tight seal
- Non-toxic, non-drying, non-hardening
- Sealant is formulated to withstand centrifugation
- No need for plastic caps or heat sealing
- Sealant's color provides a handy reference line
- Tip-Resistant tray for upright storage of 24 tubes

Ordering Information

Cat. #	Description	Unit
51602	Plain Capillary Tube, Blue Tip, 100 per vial, 10 vials per box	10 Vials
51612	Plain Capillary Tube, Blue Tip, 200 per vial, 12 vials per box	12 Vials
51608	Heparinized Capillary Tube, Green Tip 100 per vial, 10 vials per box	10 Vials
51618	Heparinized Capillary Tube, Green Tip 200 per vial, 12 vials per box	12 Vials
51628	Heparinized Capillary Tube, Calibrated at 60mm 100 per vial, 10 vials per box	10 Vials
51601	24-Place Specimen Holding Tray with Sealant	10 Trays

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Exhibit D

Diamond Line

100% PLASTIC

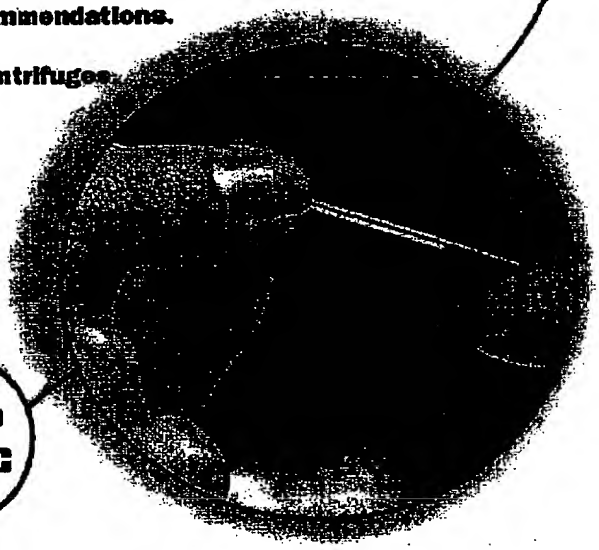
MICRO HEMATOCRIT TUBES

- **COMPLETELY UNBREAKABLE! Eliminating the risk of injury and contamination due to breakage.**
- **Eliminates the possible loss of sample and the risk of infectious disease from broken glass or mylar wrapped glass during the handling or centrifugation process.**
- **Economically priced! NO NEED TO SACRIFICE SAFETY BUYING MYLAR COATED TUBES.**
- **Contains the same capillary action and dimensional tolerances as our glass hematocrit tubes.**
- **Complies with FDA, NIOSH, CDC and OSHA safety recommendations.**
- **Designed for use in conventional 75mm hematocrit centrifuges.**
- **Private label available.**

Dimensions:
ID: 0.90±0.05 mm
OD: 1.60±0.05 mm
Length: 75±0.5mm
Volume: 45µl

Three Types of Tubes Available:
- **Untreated - Blue Tip**
- **Ammonium Heparinized - Green Tip**
- **Sodium Heparinized - Red Tip**

Packaging:
100 tubes per vial - 10 vials per box (1000 tubes per box)



Ordering Information

Cat. #	Description	Unit	List Price Per Unit
51680	Plastic Microhematocrit Tube - Untreated Blue Tip, Blue Tip, 100 per vial, 10 vials per box	10 Vials	$69.40
51684	Plastic Microhematocrit Tube - Ammonium Heparinized, Green Tip, 100 per vial, 10 vials per box	10 Vials	$69.40
51686	Plastic Microhematocrit Tube - Sodium Heparinized, Red Tip, 100 per vial, 10 vials per box	10 Vials	$69.40
51601	24-Place Specimen Holding Tray with Sealant	10 Trays	$19.00

Glass microhematocrit tubes are also available at very competitive prices. Please call our sales department for more information: (800) 394-4562.

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